

B1
40 59. (New) Host bacterium according to claim 57, characterized in that the nucleic acid
section (v) codes for the transporter domain of the AIDA protein or a variant thereof. --

REMARKS

Claims 1-19 and 41-59 are pending.

The amendment is made to put in the claims that applicants want examined.

For the convenience of the Examiner, the correspondence of the currently pending claims
and the original claims is shown in the table below.

<u>Original Claim</u>	<u>Corresponding Pending Claim</u>
1-19	1-19
20	41
21 (now cancelled)	None
22	42
23 (now cancelled)	None
24-40	43-59

Please note that the original claim 20 is presented as claim 41 with an amendment.

Similarly, claim 38 is presented as claim 57 with an amendment.

In response to the Restriction Requirement dated March 20, 2000, applicants elect with
traverse to prosecute Group I, claims 1-19, 44 (corresponding to the original claim 25) and 55-59.

In response to the election of species requirement, applicants elect with traverse the
transporter domain of the AIDA protein of E.coli (species A, claims 3, 20 and 59) and the

passenger protein of the new claim 43 (i.e. the original claim 24), where the passenger protein present in the fusion protein "is a peptide or polypeptide having an affinity for a binding partner, or is a ligand, a receptor, an antigen, a toxin-binding protein, a protein with enzymatic activity", etc.

Applicants traverse the restriction requirement because Group II is part of the same inventive concept as Group I, especially since in the new claim 41 the transporter domain of the autotransporter is specified as the AIDA protein from *E. coli*. Similarly, new claim 55 now states that the AIDA protein is encoded by the vector.

Additionally, applicants traverse the restriction requirement because the inventive concept linking the two sets of claims of Groups I and II is not taught by Francisco et al. (W093/10214).

An important feature of the present invention is that the process for the presentation of peptides on the surface of gram-negative host bacteria entails the use of an autotransporter. Such an autotransporter is fused to the passenger which can actually move through it as through a pore. W093/10214 does not use or mention autotransporters but tripartite fusion proteins which include e.g. the well-known OmpA polypeptide fused to Lpp. These transmembrane proteins do not form a pore, but instead translocation is believed to occur by membrane rearrangement. This theory has been known for some time (Georgiou et al., *Protein Eng.*, vol. 9, pp. 239-247, 1996). Thus, the mechanism of presentation of the peptides on the surface of gram-negative host bacteria in the present invention is quite different from the mechanism taught by Francisco et al.

Another difference between the present invention and the teachings of Francisco et al is that the system of the present invention uses only two components for the fusion protein, i.e. an autotransporter and a passenger, whereas in W093/10214 three different domains are fused together. Fusing three different domains has the disadvantage that correct folding of the fusion protein cannot be ensured.

Furthermore, applicants note that, in Francisco et al., the passenger is bound via its N-terminus, whereas the passenger of the present invention is bound via its C-terminus.

Another feature of the present invention is that the peptides presented on the surface of the bacterium can be cleaved off via a protease recognition site. In contrast, the fusion proteins of Francesco et al are not designed to be cleaved.

With the above differences between the claimed invention and the teachings of Francisco et al, applicants submit that the claimed invention is a contribution over the prior art. Thus, the claims of Groups I and II belong to the same general inventive concept by sharing the same or corresponding special technical feature. As a result, the claims of Groups I and II have unity of invention. Applicants request that the lack of unity of invention holding be withdrawn.

Applicants also request that the new claim 51 (the original claim 32) be joined with the elected Group I for examination on the merits. The new claim 51 is directed to a process characterized in that the modification is a proteolysis. The term "polypeptide" as mentioned in claim 43 would cover polypeptides that have been modified by proteolysis.

Conclusion

With the above amendments and reasoning, applicants submit that the present response is fully responsive to the Restriction Requirement.

In case this paper is not timely filed, the undersigned hereby petitions for an appropriate extension of time. In the event that any fees are due in connection with this paper, please charge our Deposit Account No. 01-2300.

Respectfully submitted,
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Attorney Docket No.: 100564-08019

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